Human Reproduction, Vol.25, No.6 pp. 1471–1480, 2010
Advanced Access publication on March 25, 2010 doi:10.1093/humrep/deq030

human reproduction

ORIGINAL ARTICLE *Psychology and counselling*

Predictors of psychological distress in patients starting IVF treatment: infertility-specific versus general psychological characteristics

Uschi Van den Broeck[1,2,*], Thomas D'Hooghe[1], Paul Enzlin[3], and Koen Demyttenaere[2]

[1]Leuven University Fertility Centre (LUFC), University Hospital Gasthuisberg, Herestraat 49, 3000 Leuven, Belgium [2]Department of Psychiatry, University Hospital Leuven, Leuven, Belgium [3]Institute for Family and Sexuality Studies, University Hospital Leuven, Leuven, Belgium

[*]Correspondence address. Tel: +32-16-34-28-60; Fax: +32-16-34-36-07; E-mail: uschi.vandenbroeck@uzleuven.be

Submitted on September 8, 2009; resubmitted on January 12, 2010; accepted on January 15, 2010

BACKGROUND: The distress that couples experience in IVF treatment is well-documented though research exploring factors that might contribute to the distress is scarce and the role of infertility-specific versus more general psychological characteristics in predicting psychological distress remains unexplored. This exploratory study aimed to describe, explore and test a self-constructed conceptual framework designed to understand the relative impact of infertility-specific and general psychological characteristics, in predicting psychological distress.

METHODS: Validated self-report questionnaires that measured the concepts of the encompassing framework (personality characteristics self-criticism and dependency, attachment in the partner relationship, child wish, coping, intrusiveness, infertility-related stress and general psychological distress) were completed by 106 women and 102 men before starting the first IVF/ICSI treatment at a university hospital-based fertility centre. Data were analysed by hierarchical multivariate linear regression analysis and path analysis.

RESULTS: The overall conceptual psychological framework explained 55% of the variance in psychological distress. The strongest predictors of psychological distress were general psychological characteristics: passive and active coping, self-criticism and dependency and intrusiveness. A path analysis confirmed the framework and highlighted the mediating role of coping and intrusiveness. In the final analysis, none of the infertility-specific variables significantly predicted psychological distress.

CONCLUSIONS: The current study of patients starting IVF-treatment demonstrated that general psychological characteristics, specifically active and passive coping, personality characteristics, dependency and self-criticism and intrusiveness, are more important in predicting the variability in psychological distress than infertility-specific concerns. The results raise important questions for infertility counselling. However, the cross-sectional nature of the study only allows for insight into baseline measurement (before starting the first IVF-treatment) and therefore this area of research could benefit from additional longitudinal studies.

Key words: IVF/ICSI / psychological distress / intrusiveness / coping / personality characteristics

Introduction

The inability to conceive children is experienced by individuals and couples as highly stressful (Cousineau and Domar, 2007) and the distress is well-documented (Wright *et al.*, 1989; Domar *et al.*, 1990; Leiblum and Greenfield, 1997). Qualitative studies on the psychological consequences of infertility present infertility as a devastating experience, especially for women (Greil, 1997). Quantitative studies, however, have produced more equivocal results with some studies indicating elevated levels of depression and anxiety (Domar *et al.*, 1990, 1992; Thiering *et al.*, 1993) whereas others (Freeman *et al.*, 1985; Connolly *et al.*, 1992; Hynes *et al.*, 1992) found no significant differences in an infertility population compared with the general population on standard psychological assessment.

Recent studies (Thiering *et al.*, 1993; Visser *et al.*, 1994; Slade *et al.*, 1997; Demyttenaere *et al.*, 1998; Stoleru *et al.*, 1999; Klonoff-Cohen *et al.*, 2001; Smeenk *et al.*, 2001; Verhaak *et al.*, 2001; Eugster *et al.*, 2004; Anderheim *et al.*, 2005; Boivin and Schmidt, 2005; De Klerk *et al.*, 2008) have investigated whether the distress patients experience negatively affects conception rates and treatment outcome—which

could have important implications for psychological interventions—but the association remains equivocal. Cousineau and Domar (2007) reviewed 24 studies and concluded that, though methodologically flawed, two-thirds of these studies found a significant relationship between distress and conception rates. However, a recent prospective study (Lintsen *et al*., 2009) did not find any influence of distress on treatment outcome.

Regardless of both the clinical level of distress and its possible impact on conception rates, a greater understanding of the factors that might contribute to psychological distress before starting IVF-treatment could prove to be valuable to health professionals to identify those patients in greater need of support and guide therapeutic work. Most studies (for example: Dunkel-Schetter and Lobel, 1991; Terry and Hynes, 1998; Mindes *et al*., 2003; Verhaak *et al*., 2005; Schmidt *et al*., 2005) on the psychosocial factors involved in infertility treatment originated from stress and coping theories in health psychology and were applied to infertility to give insight into vulnerabilities for distress and the conditions under which infertility is likely to be perceived as stressful, as well as factors likely to facilitate or impede adjustment to infertility. However, infertility is not only widely regarded as an uncontrollable, chronic stressor but also as a developmental life crisis (Stanton and Dunkel-Schetter, 1991) as infertility may impede the acquisition of generativity, a concern with establishing and guiding the next generation, which Erikson (1963) postulated as a central developmental task of adulthood. According to Blatt and Bass (1996), the ability to negotiate problems concerning generativity may depend on the balance that individuals can achieve between relatedness (which leads to the capacity to form mature, complex and satisfying interpersonal relationships) and self-definition (which refers to the development of increasingly differentiated, integrated and essentially positive sense of self). Vulnerability occurs when there is too much emphasis on the development of one capacity at the neglect of the other, in other words when there is an imbalance between the self-definition line and the relatedness line. Blatt and Bass (1996) coined the personality characteristics of self-criticism and dependency to refer to this type of imbalance. Self-criticism involves excessive self-evaluative concerns combined with a strong emphasis on high personal standards at the expense of interpersonal relationships. Dependency is characterized by preoccupation with interpersonal relationships and concerns about obtaining reassurance and love, at the expense of developing a clear and stable self-concept (Blatt, 2004). In this way, self-criticism and dependency could be positively associated with psychological distress.

In conclusion, though each theoretical approach to infertility (the stress and coping approach and the developmental approach) has been studied separately, there is a scarcity on literature integrating these two theoretical approaches to infertility.

In order to explore the determinants of psychological distress we constructed a comprehensive conceptual framework which will be presented in Fig. 1. The framework integrates concepts from a stress theory approach with concepts from a developmental approach thereby situating fertility problems in a broader model of psychological development across the life span (Blatt and Bass, 1996; Blatt, 2004). It consists of four levels, on the one hand more basic intra- and interpersonal characteristics to general psychological distress and, on the other from the more specific appraisal of the wish for a child to the infertility-specific concerns and general distress caused by the infertile status. Therefore, the framework includes both general psychological characteristics as well as infertility-specific concerns.

The first level of the framework, starting with the general psychological characteristics, represents the more basic intra- and interpersonal characteristics, namely personality characteristics of self-criticism and dependency and attachment in the partner-relationship. These concepts originate from the developmental framework described above and are shaped by the individual's personal and interpersonal history. They can determine, in part, how developmental milestones such as child wish and parenthood are appraised. To date only one group of researchers has studied the personality dimensions of self-criticism and dependency in an infertility population. Lowyck *et al*. (2009a, b) studied self-criticism and dependency in women starting their first IVF-treatment and concluded that they were significantly negatively associated with psychological well-being, over and above demographical variables, fertility characteristics and negative life events in the past 6 months.

The concept of attachment in the partner-relationship—the individual's typical pattern of relating to the partner—was included in the framework to represent the link between the couple relationship and distress. Attachment was already described by Bowlby (1969) as thought to determine how people cope with and adjust to stressful life events and it seems plausible to consider infertility as a stressor that has the capacity to activate attachment patterns (Feeney, 1999). In an infertility sample, Amir *et al.* (1999) found that secure attachment style was a moderator for psychological well-being and an important resource for individuals in times of stress. In addition, Lowyck *et al*. (2009a, b) found that self-criticism and dependency were negatively associated with, and romantic attachment to the partner was positively associated with well-being in men and women undergoing IVF.

A second level of the framework concerns coping. Lazarus and Folkman's (1984) transactional stress and coping paradigm provides insight into how individuals deal with stressful life events, such as infertility. Stressful events are construed as person-environment transactions around two critical processes, namely primary and secondary appraisal. Primary or cognitive appraisal is a person's evaluation of the significance of a stressor, for example, infertility is likely perceived as stressful by those for whom parenthood is appraised as a central life goal, whereas those for whom parenthood is not as central, infertility might not be appraised as particularly stressful and therefore these individuals might be less susceptible to develop psychological distress. Secondary appraisal is an assessment of the person's coping resources and options of dealing with the stressor, for example, infertile couples might seek treatment, engage in support groups or talk about their emotions with a spouse to deal with their infertility. It has been suggested that coping may serve as a mediator or buffer for psychological distress (Edelmann *et al*., 1994) though this was never researched in relation to the personality characteristics self-criticism and dependency.

A third level of the framework represents the subjective impact of infertility in specific domains. The concept of intrusiveness can be situated on this level as a symptom of the degree in which infertility is perceived as traumatic or intrusive. It is therefore a general psychological characteristic as it deals with the way in which information is processed in terms of avoidance and intrusiveness. Furthermore, intrusiveness relates to the Lazarus and Folkman's (1984) model as an outcome of the primary and secondary appraisal process: the more

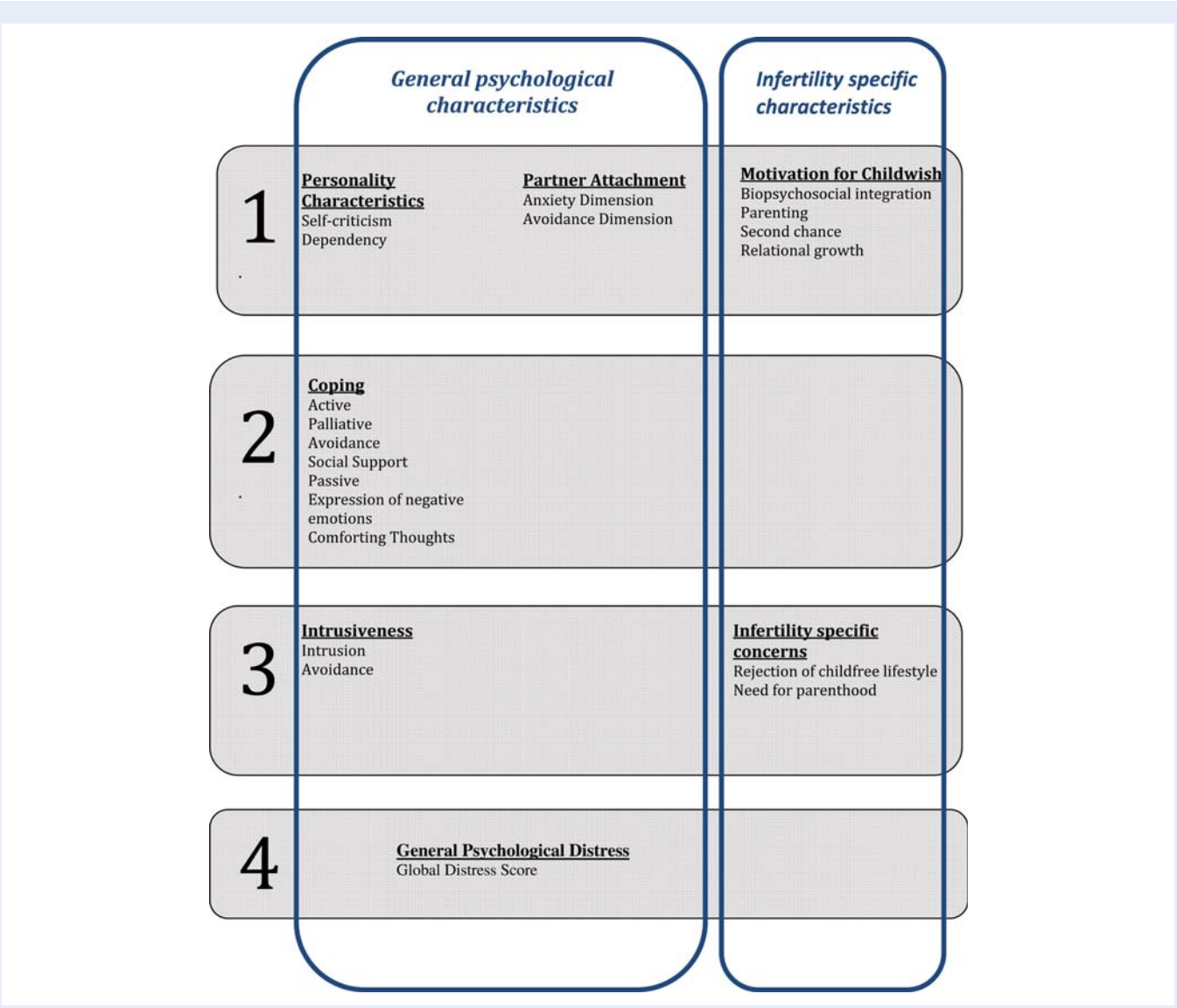

Figure 1 Conceptual psychological framework that represents four levels and includes general psychological and infertility-specific characteristics.

threatening it is for a person to have infertility problems (primary appraisal) and the more that coping resources are ineffective to deal with such a stressor (secondary appraisal), the more intrusive the infertility experience will be perceived. Anecdotal reports and clinical experience certainly support the idea that infertility is experienced as a highly intrusive event, often leading to avoidance and intrusive thoughts. Many couples report difficulty attending baby showers and may start to avoid many other pregnancy- or baby-related events, while for some the intrusiveness of the infertility experience starts to dictate their lives as they cannot stop thinking about it. Although it is well-known from clinical practice (Cousineau and Domar, 2007) that techniques such as oocyte pick-up or the timely delivery of a sperm sample can be experienced as extremely intrusive for many couples, this kind of intrusiveness has up until now never been quantified.

Finally, on the fourth level general psychological distress and complaints can be found. Generalized distress can be observed through symptoms such as sleeping problems, anxiety, crying etc. and is usually measured by standard psychological assessment.

The infertility-specific characteristics, namely motivation for child wish and infertility-specific concerns, can be found on the right hand side of the framework.

The motivation for child wish is a multifactorial concept that intertwines, often inexplicit, individual, relational and societal motives. The wish for a child was placed on the first level of the framework because it can be shaped by the person's intra- and interpersonal history and influenced by the personality characteristics and attachment. Furthermore, it can have a profound impact on how infertility is appraised—as mentioned above in the primary appraisal of Lazarus and Folkman's model. Within our framework, the motivation for the wish for a child is thought to determine how infertility is dealt with and consequently on the general and specific distress the experience can evoke.

Finally, the infertility-specific concerns, on the third level of the framework, embody the idea that specific infertility-related stress such

as, amongst others, concerns about the partner relationship, sexual and social life, might play a crucial part in the development of psychological distress. Unfortunately, as some authors (Berg and Wilson, 1990; Newton et al., 1999; Edelmann and Connolly, 2000) point out, these various specific infertility-related domains are often neglected in research on psychological outcomes of infertility. Furthermore, it has been suggested (Slade et al., 2007) that infertility-specific distress can potentially lead to more generalized distress as individuals begin to experience psychological complaints (anxiety, depression, etc.) in relation to other, non-infertility related, areas of their lives.

In conclusion, the different levels of the model integrate concepts from stress theory research and theories that place infertility as a life stressor in a broader developmental framework. The variables in the framework can be seen as distinct factors that are believed to have an impact on psychological distress. For example, the personality characteristics of self-criticism and dependency and attachment are thought to influence how individuals deal with stressful life events in terms of coping and can have an impact on how intrusive the experience is perceived. Furthermore, the proposed framework allows to compare the relative importance of more general psychological characteristics versus infertility-specific characteristics in predicting psychological distress which—to the best of our knowledge—no study has investigated within a comprehensive conceptual framework. The current study aimed to investigate the association between the different concepts in the framework. It seems evident that understanding the black box of factors that may predict the development of psychological problems may well be useful in shaping therapeutic intervention.

This exploratory study aimed to describe, explore and test a self-constructed conceptual framework that is helpful to understand the relative impact of infertility-specific and general psychological characteristics in predicting psychological distress in patients starting IVF treatment.

Materials and Methods

Participants

Women and men were eligible for the study if they met the following inclusion criteria: (i) being in a heterosexual relationship for at least 1 year, (ii) starting a first IVF or ICSI treatment with their own gametes. Exclusion criteria were as follows: (i) having had previous IVF or ICSI treatment, (ii) insufficient knowledge of Dutch to fill out the questionnaires, (iii), severe medical conditions that could interfere with baseline measurement (such as multiple sclerosis, HIV, mucoviscidosis etc.).

Patients were recruited at the Leuven University Fertility Centre (LUFC)—a tertiary, university based fertility centre in Belgium—between October 2007 and July 2008 as part of a larger ongoing prospective, longitudinal study. During the recruitment period all patients who met with the inclusion criteria were asked to participate in the study.

Procedure

This study was approved by the ethical committee of the University of Leuven (Belgium). Patients eligible for the study were sent a study package which included: a patient information sheet and a short study brochure, two consent forms (women and men) and the study questionnaires. All patients attend an intake consultation before starting the first IVF or ICSI treatment at the LUFC, therefore this was the homogenous starting point for the baseline measurement. Patients were asked to fill out the questionnaires within 2 weeks following the intake interview and to return the questionnaires to the researcher in a closed and pre-paid envelope.

Measurements

Each variable of the conceptual framework (Fig. 1) was measured and studied by (at least) one self-report measure. The variables were divided into five general psychological characteristics (personality characteristics, attachment, coping, intrusiveness and general psychological distress) and two infertility-specific characteristics (motivation for child wish and infertility-specific concerns). Socio-demographic characteristics were obtained using a short self-constructed questionnaire. The following validated psychometric questionnaires were used.

Level 1

Personality dimensions: self-criticism and dependency

The Depressive Experiences Questionnaire (DEQ; Blatt et al., 1976) consists of 66 items, scored on a seven-point Likert-type scale, ranging from 1 'I do not agree' to 7 'I totally agree' and measures the personality factors Self-Criticism and Dependency for which a global score is obtained. The Dutch version of the DEQ has good internal consistency and validity, similar to the original DEQ (Luyten et al., 1997). In our sample the reliability coefficient is 0.80 for both subscales.

Attachment in the partner relationship

The Experiences in Close Relationships-Revised (ECR-R; Fraley et al., 2000) is a revised version of Brennan et al. (1998) ECR questionnaire. It consists of 36 items and is designed to assess via two subscales the individual differences with respect to attachment-related anxiety (i.e. the extent to which people are insecure versus secure about their partner's availability and responsiveness) and attachment-related avoidance (i.e. the extent to which people are uncomfortable being close to others versus secure depending on others). The questionnaire is scored on a seven-point Likert-type scale ranging from 1 'completely disagree' to 7 'completely agree'. The reliability coefficients for our study population are 0.83 for the anxiety subscale and 0.76 for the avoidance subscale which is somewhat lower than the reliability coefficients reported in the questionnaire package (0.90 for both subscales).

Motivation for child wish

The Child Wish Questionnaire (CWQ: Bruffaerts et al., 2001) was developed to assess 'The Wish for a Child'. Consisting of two parts, the CWQ assesses motives for wanting children (CWQ-PRO) and for not wanting children (CWQ-CONTRA). For the current study, the CWQ-PRO scale was used. It consists of 101 items to be rated on a five-point Likert scale. Five motives for wanting children were identified: biopsychosocial integration, parenting, second chance, relational growth and rejuvenation. The Cronbach's alphas for the five pro-scales in our study population are, respectively, 0.85, 0.87, 0.69, 0.85 and 0.46. The rejuvenation scale was deleted due to the low internal consistency (a cut-off of 0.60 was used for minimum good internal consistency).

Level 2

Coping

The Utrechtse Coping List (UCL; Schreurs et al., 1984) consists of 47 items, scored on a four-point Likert-type scale ranging from 1 ('never') to 4 ('very often'). The UCL measures habitual coping styles. It consists of seven scales for which the reliability coefficients are given for the study sample: active coping (7 items/$\alpha = 0.84$), palliative coping (8

items/$\alpha = 0.80$), avoidance (8 items/$\alpha = 0.69$), seeking social support (6 items/$\alpha = 0.86$), passive coping (7 items/$\alpha = 0.82$), expression of negative emotions (3 items/$\alpha = 0.62$) and comforting thoughts (5 items/$\alpha = 0.78$). It has been well validated in the Dutch population and has good internal consistency and validity.

Level 3

Intrusiveness of the infertility experience

The Impact of Event Scale (IES; Horowitz *et al.*, 1979) is a short, easily administered self-report questionnaire of 15 questions, scored on a four-point Likert-type scale (0, never; 1, rarely; 3, sometimes; 4, often). It is an appropriate instrument to measure the subjective response to stress related to a specific event. It has a subscale for intrusion (intrusive thoughts, nightmares, intrusive feelings and imagery) and avoidance (numbing of responsiveness, avoidance of feelings, situations and ideas) as well as a total subjective stress score. For this study, the total subjective stress score was used and the reliability coefficient for our study sample was good ($\alpha = 0.89$).

Infertility-specific concerns

The Fertility Problem Inventory (FPI; Newton *et al.*, 1999) is a 46-item questionnaire measuring levels of infertility stress. All items are scored using a six-point Likert scale ranging from 1 (I do not agree) to 6 (I totally agree). The subscales are: social concerns, sexual concerns, relationship concerns, rejection of childfree lifestyle and need for parenthood.

The FPI was translated to Dutch according to guidelines of International Test Commission (Hambleton, 1994). The FPI demonstrates good discriminant and convergent validity (Newton *et al.*, 1999). In our study population the Cronbach's alphas for the subscales are, respectively, 0.28, 0.58, 0.51, 0.85 and 0.75. Though the social, sexual and relationships concerns subscales have clinical relevance they were not used in the analysis due to poor internal consistency, indicating high measurement error (cut-off = 0.60).

Level 4

General psychological distress

The Brief Symptom Inventory (BSI; Derogatis and Spencer, 1982) is a self-report questionnaire that surveys the presence or absence and severity of 53 psychiatric symptoms experienced in the previous week. The instrument, yields a global scale for psychological distress. The Dutch version of the BSI (de Beurs and Zitman, 2006) has good internal consistency and validity and the reliability coefficient for the global scale was good for our study sample ($\alpha = 0.96$).

Data analysis

T-tests were used to find significant differences between the responders and non-responders on the following variables: age, type of infertility, marital status, female and male medical pathology and duration of infertility. In order to find significant predictors for psychological distress a hierarchical stepwise multivariate linear regression analysis was performed on the conceptual framework, using the Statistics Package for the Social Sciences (SPSS) version 16.0. To control for gender effect, this variable was entered in a first block of the hierarchical analysis. Then, the variables in the first three levels were entered in a second block as independent variables and psychological distress as the dependent variable. Afterwards, each level was entered in to the regression analysis separately, each time controlling for the effect of gender. In total, 19 comparisons of independent-dependent variables were analysed. With such a large number of comparisons the issue of multiple testing requires some attention. A correction for multiple testing was performed with an α-level of 0.05 with the following formula: $[1 - (0.95)^{\text{number of comparisons}}]$ for the odds of one predictor being significant by chance. Then, $(y)^{\text{number of significant predictors}}$ shows the odd of all significant predictors being significant by chance.

Finally, a path analysis (using LISREL 8.72 (SSI)) and according to the method described in Kline (1998) was used to test the self-constructed framework with the significant predictors for psychological distress that were retained in the multivariate regression analysis. The value of path analysis is that it gives insight into how the predictors are inter-related directly or indirectly to the outcome variable of psychological distress. In this way, potential underlying processes or mechanisms of psychological distress can be uncovered within the proposed framework. Predictors can be directly associated with the outcome measure or indirectly (i.e. they are strongly associated with a factor which itself is strongly associated with the outcome measure). In path analysis no absolute standards can be found in the literature regarding sample size (Kline, 1998). However, there is some consensus on the ratio of the number of cases in the study to the number of parameters used in the study. Kline (1998) recommends a preferred ratio of 20:1 in order to obtain realistic goodness-of-fit measures. A minimum of $P \leq 0.05$ was considered statistically significant.

Results

Demographic and descriptive statistics

Response rate: responder non responder data

In total 450 questionnaires were sent and 208 patients (106 women; 102 men) agreed to participate in the study (response rate: 46%). However, since the study is still on-going the response rate may be an underestimation. No significant differences were found when comparing responders to non-responders concerning age, type of infertility, marital status, female and male medical pathology and duration of infertility.

Levels of distress of patients (BSI total score compared with norms)

On average the total general distress score on the BSI for the study population was 0.40 (SD = 0.42). There were no clinically significant differences with the published norms (de Beurs and Zitman, 2006) for the general Dutch population ($x = 0.42$; SD = 0.40). A summary of demographic and biomedical data of the study population is shown in Table I.

Multivariate linear regression analysis

In order to find significant predictors for psychological distress in the exploratory conceptual framework, a hierarchical stepwise forward multivariate linear regression analysis was performed on the whole model with level one, two and three taken together as independent variables and psychological distress as dependent variable while controlling for the effect of gender. The results for the overall model demonstrated that the variables Passive Coping (UCL; $\beta = 0.44$, $P < 0.05$), Self-Criticism and Dependency (DEQ; $\beta = 0.26$, $P < 0.05$ and $\beta = 0.21$, $P < 0.05$) were significant positive predictors for psychological distress. In addition, seeking Social Support (UCL; $\beta = -0.29$, $P < 0.05$) was a significant negative predictor for psychological distress. The overall model—with level one, two and three taken together—explained 55% of the variance in psychological distress, measured by BSI ($P = 0.00$).

To test the predictive value of each of the different levels of the model on their own, a multivariate linear regression analysis was

Table I Demographic and biomedical data of the study population ($n = 208$)

Gender (*n*)	
Female	106
Male	102
Educational Level (%)	
Secondary School	40
Graduate School	35
University	17
Other	8
Duration of relationship (mean in years)	7
Marital status (%)	
Married	58
Living together with legal contract	17
Living together without legal contract	25
Infertility (%)	
Primary	85
Secondary	15
Aetiology of infertility as perceived by patients (%)	
Female	22
Male	28
Both	22
Unexplained	23
Others (stress, age, miscarriage, . . .)	5

performed with psychological distress as dependent variable and level one, two and three separately as independent variables. The variables in the first level of the model (self-criticism and dependency, child wish motivations and attachment in the partner relationship) explained 37% of the variance in psychological distress ($P < 0.001$). Significant positive predictors were self-criticism, dependency and anxiety attachment with beta-values of 0.37, 0.29 and 0.12, respectively. The second level (coping) explained 50% of the variance in psychological distress ($P < 0.001$). Passive coping was a significant positive predictor whereas active coping and seeking social support were significant negative predictors with beta-values 0.61, −0.16 and −0.16, respectively. The third level (intrusiveness and infertility-related stress) explained 32% of the variance in psychological distress ($P < 0.001$). Intrusiveness of the infertility experience and need for parenthood were significant predictors of psychological distress with beta-values 0.46 and 0.17, respectively. For each analysis gender was retained as a significant predictor with beta-values of −0.15, −0.09, −0.15 and −0.03, respectively. However, when comparing the results of the hierarchical multivariate regression analysis to a multivariate analysis that did not control for gender, on the whole the same predictors were retained with comparable beta-values indicating that gender did not mediate the relationship between the independent variables and the outcome variable. Interestingly, only for active coping a decrease in beta-value was observed from −0.27 in the non-controlled regression analysis to −0.16 in the hierarchical gender-controlled analysis. For this variable, there is some evidence to suggest that gender did mediate the effect of active coping on psychological distress: when controlling for gender, high levels of active coping were still associated with lower levels of psychological distress but the association was only half as strong as in the gender uncontrolled analysis.

A possible bias in the number of significant predictors found can exist due to the large number of paired comparisons. A correction for multiple testing was calculated and demonstrated that there is a 2% chance (with a significance-level of 0.05) of finding the eight predictors in the model significant by coincidence. Consequently, it seems reasonable to claim that the eight predictors that were found significant are not a construct of the large number of comparisons in the analysis.

In summary, the proposed psychological model integrating three levels of psychological functioning to predict psychological distress explained more variability in psychological distress than each of the levels separately. Eight significant predictors for psychological distress were retained with hierarchical multivariate linear regression analysis after controlling for gender: seven predictors (Passive Coping, Active Coping and Social Support—UCL), Self-criticism and Dependency (DEQ), Intrusiveness (IES) and Attachment Anxiety (ECR-R) were general psychological characteristics whereas only one infertility-specific characteristics (Need for Parenthood; FPI) had predictive value.

Path analysis

The conceptual framework to determine psychological distress was further refined and tested with a path analysis for which only the eight significant predictors of the regression analysis were taken into account. Since goodness-of-fit statistics to evaluate model fit are dependent on sample size, Kline (1998) recommends to a ratio 20:1 of number of cases in the study to the number of parameters used. For our study, eight parameters were initially entered into the path analysis to calculate model fit indicating a preferred sample size of 160 respondents. The structural equations of the path analysis indicated that 53% of the variance in psychological distress could be explained by the five predictors that were retained, namely dependency, self-criticism, active and passive coping and intrusiveness whereas the infertility-specific predictor no longer contributed significantly to the model. Table II gives an overview of the correlation matrix of the final five predictors that were retained (Fig. 2).

Five direct paths illustrate the direct influence of each of the predictors on psychological distress. A positive relation with psychological distress was found for dependency ($\beta = 0.10$), self-criticism ($\beta = 0.18$), passive coping ($\beta = 0.37$) and intrusiveness ($\beta = 0.16$). However, a negative relationship was observed for active coping ($\beta = -0.20$) and psychological distress indicating that higher levels of active coping were correlated with lower levels of distress.

More interesting, however, are the indirect paths that give insight into the underlying psychological processes of the direct paths and reveal how the variables are related to each other in the model. Starting with dependency, on the first level of the framework, the path analysis shows three indirect paths leading to psychological distress; two of them are mediated by active and passive coping and one is mediated by intrusiveness. Self-criticism has two indirect paths leading to psychological distress that are mediated by passive

Table II Correlations of retained significant predictors after hierarchical multivariate linear regression analysis and path analysis.

	1	2	3	4	5	6
Psychological distress (1)	1.000	0.436**	0.494**	−0.377**	0.647**	0.559**
Dependency (2)		1.000	0.202**	−0.289**	0.473**	0.374**
Self-criticism (3)			1.000	−0.154	0.522**	0.418**
Active Coping (4)				1.000	−0.173	−0.291**
Passive Coping (5)					1.000	0.607**
Intrusiveness (6)						1.000

** Correlation is significant at the 0.01 level (2-tailed).

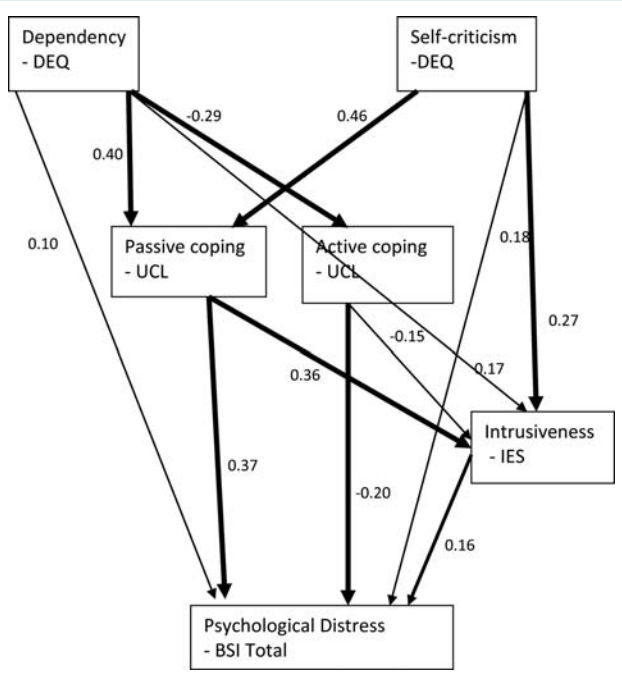

Figure 2 The diagram of the path analysis reveals both direct and indirect factors associated with psychological distress.

The figure includes beta-values, conceptually similar to correlation coefficients in that the sign represents the direction of the association and the size of the number represents the strength of the association. Bold arrows indicate a strong path (beta-value >0.20).

coping and intrusiveness. The indirect paths from the personality characteristics dependency and self-criticism clearly demonstrate the mediating role of both active and passive coping and intrusiveness to psychological distress. Furthermore, intrusiveness seems to mediate the impact of active and passive coping strategies to psychological distress.

As path analysis provides no straightforward tests to determine model fit, the best strategy for evaluating model fit is to examine multiple goodness-of-fit parameters. The statistical goodness of fit of the a-priori psychological framework was good ($\chi^2 = 2.38$; $P = 0.30$; Root Mean Square Error of Approximation: RMSEA = 0.04; Comparative Fit Index: CFI = 1.00 and Goodness of fit Index: GFI = 0.99) and therefore, the framework can be accepted.

Discussion

The current study presents and tests a self-constructed comprehensive conceptual framework to predict psychological distress in patients starting IVF-treatment. The aim of the study was to explore the associations between the variables in the model and to investigate to what extent more general intra- and interpersonal characteristics, or more specific infertility- and fertility-related characteristics, are most predictive for psychological distress in a population of patients attending an IVF clinic.

The response rate of 46% was moderate, even though this is probably an underestimation since the study is still on-going. However, there were no differences in age, type of infertility, marital status, female or male pathology or duration of infertility between responders and non-responders in the study. This seems to suggest that at least for these variables there was no selection bias between study participants and other patients starting their first IVF-treatment indicating that generalizations over the entire population are possible.

In a first step, the conceptual framework was refined using multivariate regression analysis in order to find significant predictors for psychological distress. Since no separate analysis for men and women was performed (due to sample size considerations for the path analysis), the regression analysis controlled for the effect of gender. The results certainly suggest that gender has an impact on the variability in psychological distress. Active coping was retained as a predictor in the gender-controlled analysis though its impact was considerably larger in the uncontrolled analysis. This could suggest that a gender difference exists for this variable, which is consistent with previous research (Jordan and Revenson, 1999; Schmidt *et al.*, 2005). Given the large body of evidence in the literature indicating gender differences for at least some of the variables in the framework such as coping strategies and fertility related distress (Jordan and Revenson, 1999; Newton *et al.*, 1999; Schmidt *et al.*, 2005), it seems evident that the current framework needs to be explored for men and women separately. Furthermore, the findings indicate that more general psychological characteristics (dependency, self-criticism, active and passive coping, social support, intrusiveness and attachment anxiety) are more important in predicting psychological distress than

the infertility-specific characteristics (the need for parenthood). In this way, the infertility-specific concerns and characteristics might only be secondary expressions of basic psychological dimensions. In accordance to some studies (Freeman *et al*., 1985; Connolly *et al*., 1992; Hynes *et al*., 1992) and in contrast with others (Domar *et al*., 1990, 1992; Thiering *et al*., 1993), the levels of distress in this sample were not different to those in the general population.

Interestingly, after path analysis only the general psychological characteristics (dependency, self-criticism, active and passive coping and intrusiveness) were retained. In addition, the four level structure of the model was retained in the path analysis. However, caution is warranted in interpreting causality within the path analysis due to the cross-sectional nature of the study. It would be interesting to measure possible change in the variables in the framework as patients progress through various phases of infertility treatment.

It seems safe to assert that personality characteristics of self-criticism and dependency—which are more or less stable dimensions of personality developed throughout the individual's lifetime—have an important impact on observable psychological symptoms and distress. It is well documented in the literature that in a general population these personality characteristics can predict an increased risk for developing depressive symptoms (Zuroff and Fitzpatrick, 1995; Blatt and Bass, 1996). However, the current study demonstrates that dependency and self-criticism have predictive value for general distress in an infertility population starting with IVF-treatment.

Furthermore the critical role of coping and intrusiveness as mediating variables between personality characteristics and psychological distress is highlighted.

In our sample, in regards to coping, the more participants engaged in passive coping strategies, the more psychological distress they experienced. Conversely, active coping seems to function as a buffer for psychological distress with elevated scores on the active coping strategies indicating fewer symptoms of psychological distress. However, as the gender-controlled analysis lowered the impact of active coping on psychological distress and pointed towards gender as a possible mediator between active coping and psychological distress, separate analysis should look further into possible gender differences before drawing any conclusions. In their mediating role for the personality characteristics it is interesting to note that individuals with higher scores on dependency and self-criticism also engaged more in passive coping and in turn had higher scores on psychological distress. The same was found for active coping: individuals who scored high on dependency scored lower on active coping and in turn had higher scores for psychological distress. Coping has already been well studied in the literature as a mediator for psychological distress (Benyamini *et al*., 2004; Lord and Robertson, 2005). In accordance with our findings, research on coping with infertility has suggested that the most adaptive coping strategies for addressing the problem of infertility appear to involve active problem-focused coping, social support and information seeking (Leiblum and Greenfield, 1997) as well as emotion-focused coping (Berghuis and Stanton, 2002) and acceptance of the condition. In contrast, passive coping strategies such as blaming, avoidance or denial have been linked with more maladaptive outcomes (Edelmann *et al*., 1994). In relation to infertility-specific distress, active-avoidance coping predicted high levels of infertility-specific distress for both men and women, whereas for men high levels of active-confronting coping and for women high levels of meaning-based coping predicted low levels of distress (Schmidt *et al*., 2005). In contrast with the findings of Slade *et al*. (2007) the path analysis did not reveal an association between social support and infertility-related distress or general psychological distress.

In addition, the results for intrusiveness are novel and therefore require further investigation. Intrusiveness was positioned on the third level of the conceptual framework based on the idea that it might be a correlate of the specific impact of the infertility experience and in this way it could influence general psychological distress. Our findings now certainly raise the question whether intrusiveness might not only serve as a mediator or predictor for psychological distress but may very well be a significant outcome measure to assess the adjustment to the infertility experience. Clinical experience certainly shows that the perceived impact of the infertility experience as a traumatic event is a useful approach. Indeed, infertility is considered a serious life stressor and even more, resembles in many ways the characteristics of a traumatic event with recognizable patterns of avoidance and intrusion. Furthermore, these findings can instruct specifically targeted interventions for patients who score high on intrusiveness and who are at risk of developing psychological distress. However, to the best of our knowledge no studies have been published to date on the role of intrusiveness in infertility treatment, much less in acting as a mediator for personality characteristics and coping on psychological distress.

Study limitations

Our study has several limitations. First, the cross-sectional nature of the study only allows for insight into baseline measurement (before starting the first IVF-treatment) and therefore no conclusions on causality can be drawn. To explore the direction of causality and to see how the variables in the framework may vary over the course of the infertility treatment additional longitudinal studies are required. Second, we did not control for other negative life events in the past 6 months that could have an impact on general psychological distress, other than infertility therefore a bias in our results cannot be excluded. However, Lowyck *et al*. (2009a, b) found, in their study associating self-criticism and dependency with psychological well-being that the relationship remained significant after controlling for negative life-events. Third, we did not look into gender effects in the current study due to sample size requirements for the path analysis. The hierarchical multivariate regression analysis controlled for the effect of gender on the significant predictors for psychological distress. The results certainly indicate that gender is a possible bias in the study results. At least for some of the variables in the framework such as coping, infertility-specific distress and general distress gender differences were found in previous studies (Jordan and Revenson, 1999; Newton *et al*., 1999). However, follow-up research is needed to elaborate on possible differences between men and women. Fourth, the findings are individual-based rather than analysed within the couple. Previous studies (Peterson *et al*., 2008; Lowyck *et al*., 2009a, b) have suggested interesting interaction-effects amongst partners and further work may explore these couple-effects in relation to the proposed framework. Finally, as mentioned in the results section we cannot exclude a possible bias of multiple testing. However, the magnitude of the bias has been quantified and, in light of previous findings

in the literature, the problem of multiple testing in the current study can be relativized.

Practical implications: implications for counselling

The results of the study highlight the value in addressing and targeting general psychological characteristics in infertility counselling before patients start IVF-treatment. The infertility-specific concerns and themes are overshadowed by the more general psychological characteristics. This is an interesting, novel finding with challenging implications for counselling or therapeutic practice. Our results could be interpreted in a way that addressing infertility-specific issues is useless since the more general psychological characteristics are important in predicting distress. However, caution should be exercised at ruling out infertility-specific interventions since firstly, the correlations and associations presented in the current study do not justify any assumptions on the causality of psychological interventions. More research is needed before claiming any such directions. Secondly, focusing first on infertility related issues might diminish the threshold for patients to present for counselling and therefore it can increase the acceptability of psychological interventions. Research has shown that patients have difficulties making use of a counsellor (Boivin *et al*., 1999). Talking about general psychological characteristics may not seem an appropriate topic for patients as they are dealing with such specific issues related to their infertility experiences (e.g. gender differences, social stigma, difficulty combining work schedules with treatment, guilt and shame about aetiology of infertility etc.). Thirdly, the present study can of course not answer the question whether addressing more infertility-specific levels of psychological functioning can also modulate or alter the more basic, fundamental personality characteristics.

Finally, the findings of the current study give insight into patients at risk for developing psychological distress. The final framework provides critical targets for intervention as it shows direct and indirect paths leading to psychological distress. It is important to note that even though these predictors may be of importance when patients start IVF-treatment, the crucial variables in the framework might change as patients progress through the different phases of their infertility treatment plan, allowing for a tailored approach. However, this will need to be addressed in follow-up research.

Authors' Roles

U.V.D.B., T.D., P.E. and K.D. made substantial contributions to the design and conception of this study. U.V.D.B. was involved in the acquisition, analysis and interpretation of the data. T.D. and K.D. were involved in the analysis and interpretation of the data. All authors were involved in drafting/revising and giving final approval of this article.

Acknowledgements

Myriam Welkenhuysen, clinical trial coordinator of the LUFC, made substantial contributions to this study with her support and advice on patient recruitment and data collection. Katlijne Eelen and Sarah Verschueren, midwives at the LUFC, made substantial contributions to this study with their support in patient recruitment and data collection. Furthermore, we would like to acknowledge the personnel of the LUFC, in particular the Fertility Team, for their general support and contribution to this study.

Funding

Uschi Van den Broeck has a Ph.D. fellowship of the Research Foundation—Flanders (FWO).

References

Amir M, Horesh N, Lin-Stein T. Infertility and adjustment in women: the effects of attachment style and social support. *J Clin Psychol Med Settings* 1999;**6**:463–479.

Anderheim L, Holter H, Bergh C, Möller A. Does psychological stress affect the outcome of in vitro fertilization? *Hum Reprod* 2005; **20**:2969–2975.

Benyamini Y, Gozlan M, Kokia E. On the self-regulation of a health-threat: Cognition, coping and emotions of women undergoing treatment for infertility. *Cognit Ther Res* 2004;**5**:577–592.

Berg BJ, Wilson JF. Psychiatric morbidity in the infertility population: a reconceptualization. *Fertil Steril* 1990;**53**:654–661.

Berghuis JP, Stanton AL. Adjustment to a dyadic stressor: A longitudinal study of coping and depressive symptoms in infertile couples over an insemination attempt. *J Consult Clin Psychol* 2002;**70**:433–438.

Blatt SJ. *Experiences of Depression: Theoretical, Clinical and Research Perspectives*. Washington, DC, USA: American Psychological Association, 2004.

Blatt SJ, Bass R. Relatedness and self definition: a dialectical model of personality development. In: Noam GG, Fischer KW (eds)., *Development and Vulnerabilities in Close Relationships*. Hillsdale, NJ, USA: Lawrence Erlbaum Associates, 1996. 309–338.

Blatt SJ, D'Afflitti JP, Quinlan DM. Experiences of depression in normal young adults. *J Abnorm Psychol* 1976;**85**:383–389.

Boivin J, Schmidt L. Infertility-related stress in men and women predicts treatment outcome 1 year later. *Fertil Steril* 2005;**83**:1745–1752.

Boivin J, Scanlan LC, Walker SM. Why are infertile patients not using psychosocial counselling? *Hum Reprod* 1999;**14**:1384–1391.

Bowlby J. *Attachment & Loss. Volume 1: Attachment*. London: Hogarth Press and the Institute of Psycho-Analysis. 1969.

Brennan KA, Clark CL, Shaver PR. Self-report measurement of adult romantic attachment: An integrative overview. In: Simpson JA, Rholes WS (eds). *Attachment Theory and Close Relationships*. New York: Guilford Press, 1998, 46–76.

Bruffaerts R, Enzlin P, Helsen S, Vervaeke M, D'Hooghe T, Vanderschueren D, Demyttenaere K. Early construction stages of the child wish questionnaire: factors concerning child wish and reproductive motives. *Reprod Technol* 2001;**10**:218–223.

Connolly KJ, Edelmann RJ, Cooke ID, Robson J. The impact of infertility on psychosocial functioning. *J Psychosomatic Res* 1992;**36**:459–468.

Cousineau TM, Domar A. Psychological impact of infertility. *Best Pract Res Clin Obstet Gynaecol* 2007;**21**:293–308.

de Beurs E, Zitman F. The Brief Symptom Inventory (BSI): Betrouwbaarheid en validiteit van een handzaam alternatief voor de SCL-90. *Maandblad Geestelijke Volksgezondheid* 2006;**61**:2.

de Klerk C, Hunfeld JAM, Heijnen EMEW, Eijkemans MJC, Fauser BCJM, Passchier J, Macklon NS. Low negative affect prior to treatment is associated with a decreased chance of live birth from a first IVF cycle. *Hum Reprod*. 2008;**23**:112–116.

Demyttenaere K, Bonte L, Gheldof M, Vervaeke M, Meuleman C, Vanderschueren D, D'Hooghe T. Coping style and depression level influence outcome in in vitro fertilization. *Fertil Steril* 1998;**69**:1026–1033.

Derogatis LR, Spencer PM. *The Brief Symptom Inventory: Administration, Scoring and Procedure Manual-I*. Riderwood, MD: Clinical Psychometric Research, Inc., 1982.

Domar AD, Seibel MM, Benson H. The mind/body program for infertility: A new behavioral treatment approach for women with infertility. *Fertil Steril* 1990;**53**:246–249.

Domar AD, Broome A, Zuttermeister PC, Seibel M, Friedman R. The prevalence and predictability of depression in infertile women. *Fertil Steril* 1992;**58**:1158–1163.

Dunkel-Schetter C, Lobel M. Psychological reactions to infertility. In: Stanton A, Dunkel- Schetter C (eds). *Psychological Adjustment to Infertility: Perspectives from Stress and Coping Research*. New York: Plenum, 1991, 29–57.

Edelmann RJ, Connolly KJ. Gender differences in response to infertility and infertility investigations: Real or illusory. *Br J Health Psychol* 2000; **5**:365–375.

Edelmann RJ, Connolly KJ, Bartlett H. Coping strategies and psychological adjustment of couples presenting for IVF. *J Psychosom Res* 1994; **38**:355–364.

Erikson EH. *Childhood and Society*, 2nd edn. NY, USA: WW Norton & Company, 1963.

Eugster A, Vingerhoets AJ, van Heck GL, Merkus JM. The effect of episodic anxiety on an in vitro fertilization and intracytoplasmic sperm injection treatment outcome: a pilot study. *J Psychosom Obstet Gynaecol* 2004; **25**:57–65.

Feeney JA. Adult romantic attachment and couple relationships. In: Cassidy J, Shaver PR (eds). *Handbook of Attachment: Theory, Research, and Clinical Implications*. London: The Guilford Press, 1999, 355–377.

Freeman EW, Boxer AW, Rickels K, Tureck R, Mastroianni L Jr. Psychological evaluation and support in a program of in vitro fertilization and embryo transfer. *Fertil Steril* 1985;**4**:48–53.

Fraley RC, Waller NG, Brennan KA. An item-response theory analysis of self-report measures of adult attachment. *J Pers Soc Psychol* 2000; **78**:350–365.

Greil AL. Infertility and psychological distress: a critical review of the literature. *Soc Sci Med* 1997;**45**:1679–1704.

Hambleton RK. Guidelines for adapting educational and psychological tests: a progress report. *Eur J Psychol Assess* 1994;**10**:229–244.

Kline RB. *Principles and Practice of Structural Equation Modeling*. NY: Guilford Press, 1998.

Klonoff-Cohen H, Chu E, Natarajan L, Sieber W. A prospective study of stress among women undergoing in vitro fertilization or gamete intrafallopian transfer. *Fertil Steril* 2001;**76**:675–687.

Horowitz MJ, Wilner NR, Alvarez W. Impact of Event Scale. A measure of subjective stress. *Psychosom Med* 1979;**41**:209–218.

Hynes GJ, Callan VJ, Terry DJ, Gallois C. The psychological well-being of infertile women after a failed IVF attempt: the effects of coping. *Br J Med Psychol* 1992;**65**:269–278.

Jordan C, Revenson TA. Gender differences in coping with infertility: a meta analysis. *J Behav Med* 1999;**22**:341–358.

Lazarus RS, Folkman S. *Stress, Appraisal, and Coping*. New York: Springer Verlag, 1984.

Leiblum SR, Greenfield D. The course of infertility: immediate and long-term reactions. In: Leiblum SR (ed). *Infertility, Psychological Issues and Counseling Strategies*. John Wiley & Sons, New York, 1997, 83–102.

Lintsen AME, Verhaak CM, Eijkemans MJC, Smeenk JMJ, Braat DDM. Anxiety and depression have no influence on the cancellation and pregnancy rates of a first IVF or ICSI treatment. *Hum Reprod* 2009; **24**:1092–1098.

Lord S, Robertson N. The role of patient appraisal and coping in predicting distress in IVF. *J Reprod Infant Psychol* 2005;**23**:319–332.

Lowyck B, Luyten P, Corveleyn J, D'Hooghe T, Demyttenaere K. Personality and intrapersonal and interpersonal functioning of woman starting their first IVF treatment. *Hum Reprod* 2009a;**24**:524–529.

Lowyck B, Luyten P, Corveleyn J, D'Hooghe TM, Buyse E, Demyttenaere K. Well-being and relationships satisfaction of couples dealing with an in vitro fertilization/ intracytoplasmic sperm injection procedure: a multilevel approach on the role of self-criticism, dependency, and romantic attachment. *Fertil Steril* 2009b;**91**:387–395.

Luyten P, Corveleyn J, Blatt SJ. *Dutch Version of the Depressive Experiences Questionnaire*. Leuven, Belgium: University of Leuven, 1997.

Mindes E, Ingram KM, Kliewer W, James CA. Longitudinal analysis of the relationship between unsupportive social interactions and psychological adjustment among women with fertility problems. *Soc Sci Med* 2003; **56**:2165–2180.

Newton C, Sherrard W, Glavac I. The fertility problem inventory: measuring perceived infertility related stress. *Fertil Steril* 1999;**72**:54–62.

Peterson BD, Pirritano M, Christensen U, Schmidt L. The impact of partner coping in couples experiencing infertility. *Hum Reprod* 2008; **23**:1128–1137.

Schmidt L, Holstein BE, Christensen U, Boivin J. Communication and coping as predictors of fertility problem stress: cohort study of 816 participants who did not achieve a delivery after 12 months of fertility treatment. *Hum Reprod* 2005;**20**:3248–3256.

Schreurs PJG, Tellegen B, van de Willige G. Gezondheid, stress en coping: de ontwikkeling van de Utrechtse Coping Lijst. *Gedrag: Tijdschr Psych* 1994;**12**:101–117.

Slade P, Emery J, Lieberman BA. A prospective longitudinal study of emotions and relationships in in-vitro fertilization treatment. *Hum Reprod* 1997;**12**:183–190.

Slade P, O'Neill C, Simpson AJ, Lashen H. The relationship between perceived stigma, disclosure patterns, support and distress in new attendees at an infertility clinic. *Hum Reprod* 2007;**22**:2309–2317.

Smeenk JM, Verhaak CM, Eugster A, van Minnen A, Zielhuis GA, Braat DD. The effect of anxiety and depression on the outcome of in-vitro fertilization. *Hum Reprod* 2001;**16**:1420–1423.

Stanton AL, Dunkel-Schetter C. Psychological adjustment to infertility: An overview of conceptual approaches. In: Stanton AL, Dunkel-Schetter CA (eds). *Infertility: Perspectives from stress and coping research*. New York: Plenum, 1991;3–16.

Stoleru S, Creac'h-Le Mer MN, Cornet D, Zerah S, Fermanian J, Bimbard S *et al*. Women's anxiety is a predictor of the implantation step in in-vitro fertilization [abstract]. *Hum Reprod* 1999;**14**:134.

Terry DJ, Hynes GJ. Adjustment to a low-control situation: re-examining the role of coping responses. *J Pers Soc Psychol* 1998;**74**:1078–1092.

Thiering P, Beaurepaire J, Jones M, Saunders D, Tennant C. Mood state as a predictor of treatment outcome after in vitro fertilization/embryo transfer technology (IVF/ET). *J Psychosom Res* 1993;**37**:481–491.

Verhaak CM, Smeenk JM, Eugster A, van Minnen A, Kremer JA, Kraaimaat FW. Stress and marital satisfaction among women before and after their first cycle of in vitro fertilization and intracytoplasmic sperm injection. *Fertil Steril* 2001;**76**:525–531.

Verhaak CM, Smeenk JM, Evers AW, van Minnen A, Kremer JA, Kraaimaat FW. Predicting emotional response to unsuccessful fertility treatment: a prospective study. *J Behav Med* 2005;**28**:181–190.

Visser AP, Haan G, Zalmstra H, Wouters I. Psychosocial aspects of invitro fertilization. *J Psychosom Obstet Gynaecol* 1994;**15**:35–43.

Wright J, Allard M, Lecours A, Sabourin S. Psychosocial distress and infertility: a review of controlled research. *Int J Fertil* 1989;**34**:126–142.

Zuroff DC, Fitzpatrick D. Depressive personality styles: implications for adult attachment. *Pers Indiv Differ* 1995;**18**:253–365.